Force Spectroscopy of Cell Adhesion Molecules

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Cellular adhesion molecules are placed under force during the highly specific mechanical interactions that occur between proteins and carbohydrates ligands of the cell surface/extracellular matrix. In our laboratory we have developed methods to study the elastic properties of the extracellular matrix proteins and polysaccharides at the single molecule level (1, 2, 3). We demonstrated that extracellular matrix proteins are elastic and that this elasticity involves reversible unfolding of single protein domains (1). Thus, alterations of protein elasticity may lead to pathologies in cell adhesion. Single molecule atomic force microscopy combined with protein engineering allowed us, for the first time, to measure the mechanical unfolding of a single protein module (3). These techniques also allowed us to detect mechanical phenotypes with single amino acid resolution (4). By stretching single polysaccharide molecules with AFM we have observed force-induced transitions between the chair and boat conformations of the glucose ring (2). Our measurements can detect the rearrangements of the glucose atoms with sub-angstrom resolution (2). We have postulated that these mechanical rearrangements of the functional groups may alter the reactivity of the pyranose ring acting as a switch, allowing or preventing the binding to receptors (2).

Cell adhesion molecules play critical roles in cellular development and cell-cell recognition. These molecules are the frequent target of mutations and toxins that can have a catastrophic effect on migration, morphogenesis and development. Our force spectroscopy measurements readily identify the mechanical signature of extracellular matrix proteins and carbohydrates and can be used to detect mechanical phenotypes and toxic modifications at the level of single molecules. The single molecule sensitivity of our AFM measurements can also be used to design detectors that mimic cellular adhesion recognition reactions.

References:

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